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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,953	12/10/1998	OYSTEIN FODSTAD	7885.56USWO	8358

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MERCHANT & GOULD P.C.
P.O. BOX 2903
MINNEAPOLIS, MN 55402

EXAMINER

SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/125,953

Applicant(s)

FODSTAD ET AL.

Examiner

Bradley L. Sisson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,3,6-9 and 12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,3,6-9 and 12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 20 September 2004 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 2, 3, 6-9 and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over SmithKline Beecham Corporation (WO 95/21944; SmithKline) in view of Høifødt et al. (WO 95/24648) and either Zeng et al. or Kuranami et al.

6. Smithkline, page 3, last paragraph, and pages 13-14, disclose method for conducting differential hybridization whereby genes differentially expressed in disease tissue as compared to healthy/normal tissue are identified. At page 3, lines 16-17, discloses employing these methods so to provide methods of diagnosis of diseases. By determining which genes are differentially expressed, and the level at which they are expressed, one also determines the level of mRNA expression. In support of this position attention is directed to page 3, last paragraph, and to page 13, first full paragraph, which teaches that mRNA and/or can is isolated from the biological sample from both healthy and diseased individuals. Also disclosed is the cloning of genes identified through the disclosed processes, e.g., subtractive hybridization. This meets a limitation of claims 6 and 7.

7. SmithKline does not teach immunomagnetically isolating the cells prior such that nearly 100% specific target cells are obtained, nor do they teach taking their first and second tissues from the same individual.

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8. Høifødt et al., page 3, disclose using immunomagnetic methods to not only detect but to isolate target cells in an otherwise mixed population of cells. Page 7, line 21, bridging to page 8, line 9, discloses using immunomagnetic separation for the establishment of “a pure population of target cells” such that one can examine genes at the “DNA, RNA and protein level.” The aspect of achieving “a pure population of target cells” is considered to meet the limitation that one obtains a “nearly 100% specific target cell [population].”

9. Høifødt et al., page 4, last paragraph, bridging to page 5, teach that their method of immunomagnetic separation of cells overcomes prior difficulties in being able to readily isolate diseases (e.g., malignant) cells in a heterogeneous mixture of cells. Høifødt et al., also teach explicitly that their method is “very sensitive.”

10. Høifødt et al., at pages 21-25 (Table 1) provide an exhaustive listing of antigens and antibodies that can be used to isolate specific cells, which in turn can be used or the subject of further investigation.

11. Høifødt et al., page 8, first paragraph, disclose the applicability of the immunomagnetic separation where one would be able to identify new genes associated with tumor cells, where the tumor can be malignant (page 8, line 5) and can be found in bodily fluids (page 8, line 6). This meets a limitation of claims 2 and 3.

12. Both Zeng et al. (page 575, right column, last paragraph), each using “matched” normal and malignant tissue samples. The aspect of using “matched” samples is construed as being from the same individual. Kuranami et al. (page 233, right column, last paragraph, bridging to page 234) teach isolating cancerous tissue as well as normal (adjacent) tissue from the same

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individual. The aspect of using cancerous and normal tissue samples meets the limitation of taking first and second tissues from the same individual (claim 12, step (A)).

13. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to have combined the aspect of taking a first and second tissue samples from the same individual (Kuranami et al., or Zeng et al.) and to have isolated specific target cells from said first and second tissue samples as disclosed by Høifødt et al., with the method of SmithKline as the ordinary artisan would have been able to isolate target (pathogenic) cells both easily and with a high degree of sensitivity and to then use this enriched population of cells in the subtractive hybridization assay disclosed by Smithkline whereby genes differentially expressed are identified. In view of the explicit teachings of suitable antigens and antibodies provided by Høifødt et al., and the detailed guidance as to how differentially-expressed genes can be isolated from different tissues (SmithKline), the ordinary artisan would have been amply motivated and would have had a most reasonable expectation of success. For the above reasons, and in the absence of convincing evidence to the contrary, claims 2, 3, 6-9, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the prior art of record.

Conclusion

14. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114.

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See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

15. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

17. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "B. L. Sisson". The signature is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

Bradley L. Sisson
Primary Examiner
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BLS
29 September 2004